Amendments to the Claims

Please amend the claims as indicated, with deletions indicated by strikethrough and insertions by underlining.

1-27. (Canceled)

28. (Currently Amended) A method of designing amino acid sequences of variable domains of a humanized monoclonal antibody comprising:

(a) comparing ~~determining residue identities between~~ the amino acid sequences of the light and heavy chain variable domains of a monoclonal antibody to be humanized ~~and~~ with the amino acid sequences of the ~~corresponding~~ light and heavy chain variable domains of ~~two or more~~ human antibodies;

(b) selecting framework regions from a first human antibody for the light chain and from second and third human antibodies for the heavy chain based on the sequence comparison, wherein the heavy chain FR1, FR2 and FR3 are selected from the second human antibody and FR4 is selected from the third human antibody~~from said corresponding variable domains of two or more human antibodies, at least one human antibody for the framework regions of light chains and at least one human antibody for the framework regions of heavy chains wherein the human antibody for the framework regions of the light chains is different from the human antibody for the framework region of the heavy chains and framework regions of the heavy chain have a sequence identity of at least 62.5% and framework regions of the light chain have a sequence identity of at least 69% to corresponding framework regions in the monoclonal antibody~~; and

(c) incorporating the framework regions selected in step (b) with the corresponding light and heavy chain complementarity determining regions of the monoclonal antibody to be humanized, to design a humanized light and heavy chain variable domain amino acid sequences.~~;~~

~~(d) retaining selected amino acid residues from the framework regions of the monoclonal antibody to be humanized in the corresponding framework regions of the humanized variable domain if one or more of said selected amino acids are predicted to have contacts with said complementarity determining regions affecting the affinity and specificity of the resultant humanized monoclonal antibody; and~~

~~(e) obtaining amino acid sequences of the variable domains of the light and heavy chain regions of the resultant humanized monoclonal antibody.~~

29. (Currently Amended) The method according to claim 28, further comprising retaining selected amino acid residues from the framework regions of the monoclonal antibody to be humanized in the corresponding framework regions of the humanized variable domains where said selected amino acids are predicted to have contacts with said complementarity determining regions~~wherein at least three of said framework regions are from different human antibodies~~.

30. (Currently amended) The method according to claim 28, wherein the heavy chain FR4 is selected from the human NEWM antibody~~said heavy chain framework regions are from the heavy chain regions of at least two different human antibodies~~.

31. (Currently amended) The method according to claim 29~~2~~8, wherein said selected amino acid residues ~~of step (d)~~ are within a 4.5 Angstrom radius of any atoms within a complementarity determining region~~s~~ of the light or ~~and~~ heavy chain of the ~~resultant~~ humanized monoclonal antibody.

32. (Currently Amended) ~~A method of producing a humanized monoclonal antibody designed according to the~~ The method of claim 28, further comprising~~comprising the additional steps of~~:

(d)~~(f)~~ preparing a DNA sequences encoding the humanized light and heavy chain variable domains ~~of the resultant humanized monoclonal antibody based upon the designed~~ amino acid sequences;

(e)~~(g)~~ operably incorporating the variable domain DNA sequences into at least one vector comprising DNA sequences encoding the constant domains of the human light and heavy chain regions;

(f)~~(h)~~ introducing the at least one vector into a cell; and

(g)~~(i)~~ culturing the cell containing the at least one vector ~~under conditions~~ to produce the humanized monoclonal antibody.

33-37. (Canceled)

38. (New) The method of claim 28, wherein the light chain framework regions are selected from the human REI antibody.

39. (New) The method of claim 28, wherein the heavy chain FR1, FR2 and FR3 are selected from the human EU antibody.